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Funcional properties of the upper arm vascular bed and hypertension

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Summary

The level of the arterial blood pressure depends on several cardiovascular factors. One of these factors is the compliance of blood vessels. In the absence of vessel wall changes, the vascular compliance decreases with increasing blood pressure. Conversely, the blood pressure increases with decreasing vascular compliance. Changes in blood pressure and changes in vascular compliance are therefore inextricably linked. The arterial blood pressure is generally referred to the hydrostatic level of the heart. It is usually noninvasively determined at the upper arm by measuring the systolic and diastolic blood pressures. The most frequently used methods for the noninvasive measurement of blood pressure are described in the chapter 1. In this chapter, the definitions of normotension and hypertension are examined too. The distinction between high and normal blood pressure appears to be quite arbitrary and subject to frequent changes. This is especially due to the fact that in more than 90% of the cases the origin of the hypertension is unknown. Hence, causes of hypertension can not be reckoned with in the evaluation of arterial blood pressure. The definition of hypertension is therefore largely based on the risk of morbidity and mortality associated with hypertension, and on results of pharmaceutical intervention studies.

Because of the strong relationship between changes in blood pressure and changes in vascular compliance, it seems likely that measurement of the arterial compliance may be useful in the investigation of origin, diagnosis and treatment of hypertension. In human such investigations have yielded little useful result up to now. This is due to the complex relationship between arterial blood pressure and compliance, as well as to the limitations of the available methods for measuring arterial compliance. Consequently it is difficult to establish whether observed differences in arterial compliance are caused by differences in arterial blood pressure, differences in vascular properties or both. This study therefore, concentrates in the first place on the development of a method by which differences in compliance due to differences in vascular properties, may be distinguished from those which

are due to changes in blood pressure. The method is based on electrical impedance measurements. An alternating current of low intensity is led through an arm in the longitudinal direction and the impedance of a tissue segment of the upper arm is measured. With the method not only the arterial compliance, but also other properties of the vascular bed of the upper arm segment may be investigated, such as the arterial and venous blood volumes. Therefore, the arterial distensibility, the ratio of arterial compliance and blood volume, may be calculated as well. The reciprocal values of both compliance and distensibility are frequently used to express vascular stiffness.

In chapter 2 the method is introduced and described in detail. In chapter 3 the results obtained in healthy subjects and in patients are presented. The primary aim of these measurements was to gain insight into the vascular properties of hypertensive patients. In chapter 4 finally, the consequences of the results are discussed.

In the first part of chapter 2 the general principles of the method are explained. They are illustrated by measurements on elderly volunteers using a first experimental set-up. Based on the results of these measurements, the method has been improved considerably. In the second part of the chapter the improved method is further examined, in particular with regard to its repeatability. The repeatability of the method proved to be well within the physiologically acceptable range, and of the same order of magnitude as that of established methods.

From the results of the measurements in healthy subjects, described in the first part of chapter 3, it appears that the stiffness of the larger arteries of the upper arm vascular bed increases with age. This fits in with the age-related increase in aortic stiffness, described in the literature. The effect of the age-related increase in large artery stiffness on the arterial bed as a whole appears, at least partly, to be compensated for by a decrease in stiffness of the smaller arteries. The age-related differences in arterial stiffness however, could only be demonstrated in the female, not in the male subjects. The differences between younger and older women furthermore, appear to be due to the age-related increase in body mass index rather than to aging per se. Several other properties of the upper arm vascular bed proved to be related to age, gender and body mass index. As a consequence,

comparative studies concerning vascular properties should preferably be performed in subjects matched as to age, gender and body mass index. The results of the measurements explain why older females are more vulnerable to develop isolated systolic hypertension than males. Moreover, the results show that both obese males and obese females have an increased risk to develop hypertension.

It is still often taken for granted that hypertension is accompanied by an increase in arteriolar constriction. Sometimes it is even assumed that hypertension is caused by the constriction. From the results of a comparative study of patients with mild to moderate essential hypertension and paired normotensive controls it appears, however, that an increased arteriolar constriction is quite improbable. The characteristic increase in vascular resistance during hypertension appears rather to be due to an increased constriction of the larger arteries: both volume and compliance of the larger arteries were considerably smaller in the hypertensive patients than in the normotensive controls. Arteriolar compliance and volume on the other hand, were higher. The vascular bed of hypertensive patients thus seems to protect itself efficaciously. The resistance increase of the larger arteries screens the smaller arteries from pressure overload, and the compliance increase of the smaller vessels compensates for the compliance loss of the larger arteries. It seems probable therefore, that vasoconstriction proceeds from large arteries to arterioles when hypertension progresses, instead of the other way round as is often assumed. This would also better fit in with the results of animal studies. The observed changes in the properties of veins furthermore, demonstrate that hypertension is not restricted to the arterial system. Changes in venous properties, such as an increase in venous blood volume, should therefore be considered in each study concerning the origin of arterial hypertension.

The familiar age-related increase in aortic stiffness led many to believe that isolated systolic hypertension in the elderly is a normal accompaniment of more rigid arteries, caused by the process of normal aging. However, from the results of a comparative study of patients with isolated systolic hypertension and paired normotensive controls, it appears that isolated systolic hypertension is not the result of normal aging. The observed

differences in arterial properties between patients with isolated systolic hypertension and normotensive controls resemble those between older and younger normotensive subjects, but for the differences in venous properties rather the opposite holds true. Isolated systolic hypertension could indeed be depicted as an exaggerated process of aging as far as the changes in arterial properties are concerned, but not as far as the changes in venous properties are concerned. The vascular properties of patients with isolated systolic hypertension moreover, differ considerably from those of patients with mild to moderate essential hypertension. The larger arteries of the upper arm vascular bed of patients with isolated systolic hypertension showed an increased dilatation instead of an increased constriction as in essential hypertension. The compliance of the larger arteries nevertheless was normal. This suggests an increased structural stiffness of the larger arteries which is counteracted by a decrease in the myogenic tone of the arterial wall. Again, no evidence was found for an increased arteriolar constriction: on the contrary, both volume and compliance of the smaller arteries were higher. The observed differences in vascular properties suggest, that the wall tone of the arteries as well as the veins is lowered in patients with isolated systolic hypertension.

In the last part of chapter 3, preliminary results are presented of some other investigations. Each study concerns patients with a disease which is probably associated with changes in vascular properties. The measurements are performed in (A) patients suffering from diabetes mellitus, (B) pregnant women with complicated or uncomplicated hypertension and (C) hypertensive patients under medical treatment.

(A) In a group of diabetic patients with proven peripheral macrovascular disease, changes in arterial compliance and blood volume were observed which suggest a structural narrowing of the smaller arteries. The effect of the structural narrowing on arterial compliance however, seems to be compensated for by a decrease in arterial vessel wall tone. In another group of insulin-dependent diabetics with microalbuminuria but no macrovascular disease, no changes in the compliances and blood volumes of the upper arm vascular bed were found. The heart rate and the average value of the interstitial fluid volume however, were considerably higher in the diabetics

than in the nondiabetic controls. Future research should establish the significance of these findings, in particular with regard to the origin of vascular disease and hypertension in diabetes mellitus. (B) The observed differences in vascular properties between pregnant women with and without uncomplicated hypertension, resemble those between non-pregnant patients with and without essential hypertension. This agrees with the suggestion that pregnancy-induced hypertension is a latent essential hypertension brought to light by pregnancy. In preeclamptic pregnancies however, there was increased vasoconstriction in all parts of the vascular bed. The increased vascular resistance and reduced blood volume found by others in preeclamptic pregnancies, the reduced uteroplacental perfusion in particular, fit in surprisingly well with these findings. (C) At least as noteworthy are the preliminary results of a study in which the effects of antihypertensive treatment on the vascular properties of patients with previously untreated mild to moderate essential hypertension, are investigated. After six months of active treatment all patients appeared to be normotensive. The properties of the upper arm vascular bed appeared to be changed in the direction of those of the paired normotensive controls. The compliance of the larger arteries, however, remained lower, while the venous properties remained different from those of the normotensive controls. Future research should demonstrate, to what extent the effect of antihypertensive treatment on cardiovascular risk is limited by the remaining differences in vascular properties.

In chapter 4 the impedance method is critically reviewed. For this purpose the results of the measurements are compared with those of previous measurements using other, more established methods. The consequences are discussed of the additional information which has been obtained by using the developed method, in particular with regard to hypertension. A hypothesis is put forward for explaining the observed differences in vascular properties between hypertensive patients and normotensive controls. In this hypothesis, the venous part of the circulation plays a more important part than in the usual theories. The increase in arterial blood pressure moreover, seems to be a symptom rather than a cause of the changes in large artery properties. Apart from the direct effect of blood pressure, the observed decrease in

dilatatory reserve of the smaller arteries may be responsible for the increased risk of cardiovascular disease associated with hypertension. The results of the investigations as a whole, stress the often neglected role of the larger arteries in controlling local tissue perfusion and the latter's dependence on control mechanisms operating at system level.